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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/572,635

03/17/2006

Simon Nicholas Black

056291-5237

4207

9629 7590 03/05/2009
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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

03/05/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/572,635	Applicant(s) BLACK ET AL.	
	Examiner /Venkataraman Balasubramanian/	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3/17/2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/17/2006, 09/29/2006, 10/05/2006, 10/16/2008</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Claims 1-12 are pending.

Information Disclosure Statement

References cited in the Information Disclosure Statements, filed on 3/17/2006, 9/29/2006, 10/5/2006 & 10/16/2008, are made of record.

Claim Objections

Claim 12 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim. Not claim 9 is a multiple dependent claim and claim 12 is depends on claims 9-11. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 9-12 are indefinite as it is not clear what process is claimed therein for what form. As recited, claim 9 appears to be related to form of claim 1 and claim 4. But claim 10 and 11 refers to Form 2 and Form 3 for which there is no antecedent basis.
2. Claim 7 provides for the use of the crystalline form of claim 1 or claim 4 but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it

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merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating type 2 diabetes and lowering blood cholesterol, does not reasonably provide enablement for treating any or all diseases embraced in these claims. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims.

The instant method of use claim 8 is drawn inhibition of HMG CoA using crystalline form of claim 1 or claim 4 and thereby treating any or all diseases based on the mode of action of instant compounds as HMG CoA reductase inhibitors in general.

Instant claim, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of HMG CoA reductase by the instant compounds, instant claims reaches through inhibiting and treating any or all diseases in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibition of HMG CoA reductase, based on limited assay, it is claimed that treating any or all diseases in general, which there is no enabling disclosure.

As recited, the scope of the claims can include treating hypercholesterolemia, dyslipidemia, hyperlipidemia, hyperlipoproteinemia, LDL Pattern B, LDL Pattern A, hypertriglyceridemia or atherosclerosis, or Alzheimer's disease or osteoporosis, inhibiting cholesterol biosynthesis or lowering blood serum cholesterol levels and/or modulating blood serum cholesterol levels, lowering LDL cholesterol and/or increasing HDL cholesterol, and/or lowering triglycerides, or treating dyslipidemia, mixed dyslipidemia, LDL Pattern B, LDL Pattern A, hyperlipidemia, hypercholesterolemia, hypo a-lipoproteinemia, hyperlipoproteinemia or hypertriglyceridemia, and other aberrations of apolipoprotein B metabolism, or reducing levels of Lp(a), or treating other cholesterol-related diseases, or treating or reversing progression of atherosclerosis, treating Alzheimer's disease, or treating osteoporosis and/or osteopenia, or reducing inflammatory markers, reducing C-reactive protein, or treating low grade vascular inflammation, or treating stroke, or treating dementia, and treating coronary heart disease, myocardial infarction, or treating stable and unstable angina, or primary prevention of coronary events, or secondary prevention of cardiovascular events, or treating peripheral vascular disease, preventing or treating peripheral arterial disease, or treating acute vascular syndromes, or reducing the risk of undergoing myocardial revascularization procedures, or treating microvascular diseases such as nephropathy, neuropathy, retinopathy and nephrotic syndrome, or treating hypertension, preventing

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or treating diabetes, especially Type 2 diabetes, and related diseases, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, obesity, LDL Pattern B, LDL Pattern A, Syndrome X, diabetic complications, dysmetabolic syndrome, and related diseases, and sexual dysfunction, preventing and treating malignant lesions, premalignant lesions, gastrointestinal malignancies, liposarcomas and epithelial tumors, cancer-induced asthenia (fatigue), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and gallstones, and HIV infection, drug-induced lipodystrophy, and proliferative diseases, for improving coagulation homeostasis, reducing PAI-1 activity, reducing fibrinogen, and/or reducing platelet aggregation, and/or improving endothelial function, which is not adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have HMG CoA reductase inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as HMG CoA reductase inhibitor would be useful for all sorts of diseases including cancers. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis, lung cancer, brain cancer, pancreatic cancer, colon cancer etc. are very difficult to treat and despite the fact that there are many anticancer drugs.

Proliferative disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the *Helicobacter pylori* infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

No compound has ever been found to treat proliferative diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a “compound” is contrary to our present understanding of oncology. Cecil Textbook of Medicine states, “each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study” (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

No compound has ever been found to treat all types of medical conditions or diseases generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a “compound” is contrary to our present understanding of modern medicine.

Note substantiation of utility and its scope is required when utility is “speculative”, “sufficiently unusual” or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that ‘a claimed invention must have a specific and substantial utility’. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art at the time of instant invention is indicative of the requirement for undue experimentation. See *Khan et al.*, *Diabetes Care* 25(4), 708-771, 2002 and *Iida et al.*, *FEBS Letters* 520, 177-181, 2002. See also *Rutishauser Swiss Medical Weekly*, 126, 41-49, 2006.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: The method of use claims are drawn to treating of variety of diseases and disorders. However, specification provides no support for treating all or any diseases/disorders. In fact, based on the specification and examples,

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it appears that the instant compounds are mainly HMG CoA reductase inhibitors and may be useful for lowering cholesterol and treating Type-2 diabetes. Specification has not provided any evidence or nexus that because of the mode of action of the instant compound, the compound would be useful for treating any or all said diseases/disorders and cancers. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as “showing” such utility, and not “warranting further study”). The evidence presented in this case does not show such utilities related to ‘prevention’, but only warrants further study.

2) The state of the prior art: Recent publications expressed that the inhibition effects of HMG CoA reductase are unpredictable and are still exploratory and agonists. See *Khan et al.*, and *Iida et al.*, cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating all the said diseases and any or all cancers by the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved”. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating and any

or all diseases recited in the instant claims and the state of the art is that the effects of HMG CoA reductase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace treating various diseases with huge genus of compounds.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was ‘filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion is clearly justified here and undue experimentation will be required to practice Applicants’ invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 7 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al., WO 01/60804. Taylor et al., teaches crystalline form of rosuvastatin with tris(hydroxymethyl)methylamine. See entire document. See page 3, entry 5, for crystalline form of tris(hydroxymethyl)methyl ammonium salt of rosuvastatin and pages 3-6, for details. See also page 4 lines 13-16. See examples 1-10 shown in pages 7-15.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571)

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272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624